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TETANUS

ANALYSIS OF 1458 CASES, WHICH OCCURRED IN HOME MILITARY HOSPITALS DURING THE YEARS 1914—1918

BY

SIR DAVID BRUCE, K.C.B., F.R.S.

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TETANUS.

ANALYSIS OF 1458 CASES, WHICH OCCURRED IN HOME MILITARY HOSPITALS DURING THE YEARS 1914—1918

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(With 12 Diagrams and 1 Curve.)

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INTRODUCTION.

THE purpose of this paper is to place on record the available figures relating to cases of tetanus which occurred in Home Military Hospitals during the Great War of 1914–1918. It may be considered that some of the tables give no very useful or practical information, but they are nevertheless recorded in order that medical officers at the outbreak of some future war may have the opportunity of learning what was done for the prevention and treatment of tetanus during this war. For example nothing can be gained from a study of the figures given in this analysis with regard to the curative or therapeutic value of antitetanic serum, but it may be of some antiquarian interest half a century hence to know the amount given and the mode of administration in the years 1914–1918.

The total number of British wounded in all the theatres of war has been officially reported as 2,032,142. If the number 2385 be taken as the total number of cases of tetanus which occurred among these wounded then the incidence of cases of tetanus to wounded is 1·17 per 1000.

The total number of wounded treated in Home Hospitals has been calculated to be about 1,242,000. The number of cases of tetanus arising among them was 1458, giving an incidence of 1·2 per 1000.

It is the analysis of these 1458 cases which forms the subject of this paper. It must then be distinctly understood that only cases of tetanus arising in England are dealt with. Cases occurred in France and were treated in Military Hospitals in France, among wounded soldiers, before they had an opportunity of being transferred to England. These have been analysed at least in part by Sir William Leishman and Major Smallman, and later by Colonel Cummins and Major Gibson.

Tetanus made its appearance very shortly after hostilities had commenced and it soon became evident that vigorous steps would have to be taken to save our men from this painful and very fatal disease. It had been expected, of course, that there would be a few cases of tetanus among the wounded men and provision had been made to deal with such cases when they arose. Nevertheless when it became possible to obtain figures showing the incidence of tetanus it was seen that the numbers were considerably higher than had been anticipated. Lord Kitchener, then Secretary of State for War, and the Director-General, Army Medical Services, accordingly determined to lose no time in grappling with the danger.

My connexion with this work was due to an order from the then Director-General, Sir Alfred Keogh, G.C.B., who wrote in October 1914, "It is hoped that you will direct your attention specially to the subject of Tetanus, with a view to elucidating the problems of causation and cure." Hence the taking up of this kind of work, which was quite new to me, was due to a request from the Director-General and not from any volition on my own part.

In March 1916, a Tetanus Committee was formed at the suggestion of Prof. Waller, F.R.S., the late Prof. Plimmer, F.R.S., and Captain Golla, R.A.M.C. The first meeting took place on the 7th March of that year. A Memorandam on Tetanus, which is now in its fourth edition, was prepared by the committee and circulated; the Tetanus Report forms were revised, and a special form prepared for the use of the inspectors of Tetanus. Copies of these documents are attached, as they may be found of some use in the future.

There were some forty Inspectors of Tetanus stationed in different parts of the country whose duty it was to visit cases of tetanus as soon as they occurred, and to advise or assist when necessary in the treatment. These inspectors were usually expert clinicians, neurologists or bacteriologists, and were of the greatest service in establishing sound methods in the nursing and treatment of the cases.

They sent in an independent report which was useful to compare with the report sent in afterwards by the Medical Officer in charge of the case. The inspectors were without exception all of them keen on the work, and I consider the idea of detailing officers for this purpose in every important centre in the three kingdoms to have been the most useful and most practical part in the organisation for the study and care of the cases of tetanus.

Members of the Tetanus Committee have written several papers in the Medical Journals with a view to giving medical officers the latest developments in our knowledge of tetanus. A list of these papers is given in an appendix. The Committee also instituted various original investigations. Capt. Golla, R.A.M.C., worked at different problems at the Physiological laboratory of the University of London, Capt. Tulloch, R.A.M.C., at the Lister Institute, and Prof. Sherrington in his own laboratory at Oxford. The expenses of these various researches, amounting to £1350, were borne by the Lister Institute, without which generous aid the Committee would have been unable to carry out any of this research work.

In conclusion, my best thanks are due to Lady Bruce for the immense amount of work she has undertaken in the preparation of this Analysis. To her fell the irksome task of collecting and arranging under their different heads, the various particulars contained in the Inspectors' Reports and the Tetanus Returns.

This has been an undertaking of a particularly arduous and tiresome character demanding qualities of patience and industry especially when dealing with Reports often written with extreme haste and illegibility.

I would also wish to express my best thanks to all the Inspectors of Tetanus who were, in the main, responsible for carrying out the Committee's recommendations; to the Officers Commanding Hospitals, Medical Officers in charge of cases, and to the nursing Sisters to whom falls the heaviest burden in the care of the cases.

I. THE INCIDENCE OF CASES OF TETANUS AMONG THE WOUNDED TREATED IN HOME MILITARY HOSPITALS.

In regard to the incidence of tetanus among the wounded soldiers treated in home military hospitals, it is impossible to deal at all fully. The number of wounded sent over to England from the Western Front between August 1914 and November 1918 was roughly 1,242,000. The number of cases of tetanus which occurred during this period in home hospitals was 1458. This gives a rate of incidence of 1·2 per 1000. It must be confessed that these figures can only be approximate. It will probably be years before the correct figures are available. For example many cases of "gassing" were included among the wounded. For the purpose of adjudicating pensions this may be useful but for purposes of tetanus statistics it introduces a fallacy.

Diagram 1 is an attempt to give the ratio of the number of cases of tetanus per thousand of the wounded landed in England during each month, from August 1914 to the close of the war on November 11th, 1918.

The cases of tetanus are reckoned from the date of wound not from the date of onset. For example, 2161 wounded men arrived in England from overseas during August 1914. Eight of these men were at some time attacked by tetanus, giving a ratio of 3·7 per 1000.

From this diagram it will be seen that the ratio of the number of cases of tetanus occurring in home military hospitals to the number of wounded sent over to England is 3·7 per 1000 in August 1914; 9 per 1000 in September, and that it rapidly drops to 1·4 in December, at which lower rate it continues practically during 1915. There is a tendency to rise during 1916 due it may be to an improvement in the diagnosis and subsequent increase of cases of local tetanus, which at the beginning of the war were possibly overlooked. This would naturally raise the ratio of the incidence.

It will also be seen that the incidence of the disease tends to become lower as the war goes on. It is probable that this is due after the middle of 1917 to more thorough surgical treatment. It was stated in the second analysis of cases of tetanus in 1915 that "if thorough surgical treatment is carried out on wounds from the beginning so as not to allow the presence of necrotic tissues or foreign bodies, the number of cases of tetanus should sensibly diminish if not altogether disappear." The surgeons took a long time to learn how to do this, but in the introduction of primary excision and primary or delayed primary suture the most remarkable results were obtained, and if it had not been for the sudden cessation of the war, it is probable that tetanus would have become almost extinct among the British wounded. The most interesting feature in the diagram is the sudden drop in 1914 from 9 per 1000 in September to 1·4 per 1000 in December. This was undoubtedly due to the introduction of prophylactic injections of antitetanic serum which did not come into force until about the middle of October. This topic will be discussed more fully when the prophylactic or preventive treatment of tetanus comes under review.

THE RATIO PER 1,000 OF CASES OF TETANUS TO WOUNDED

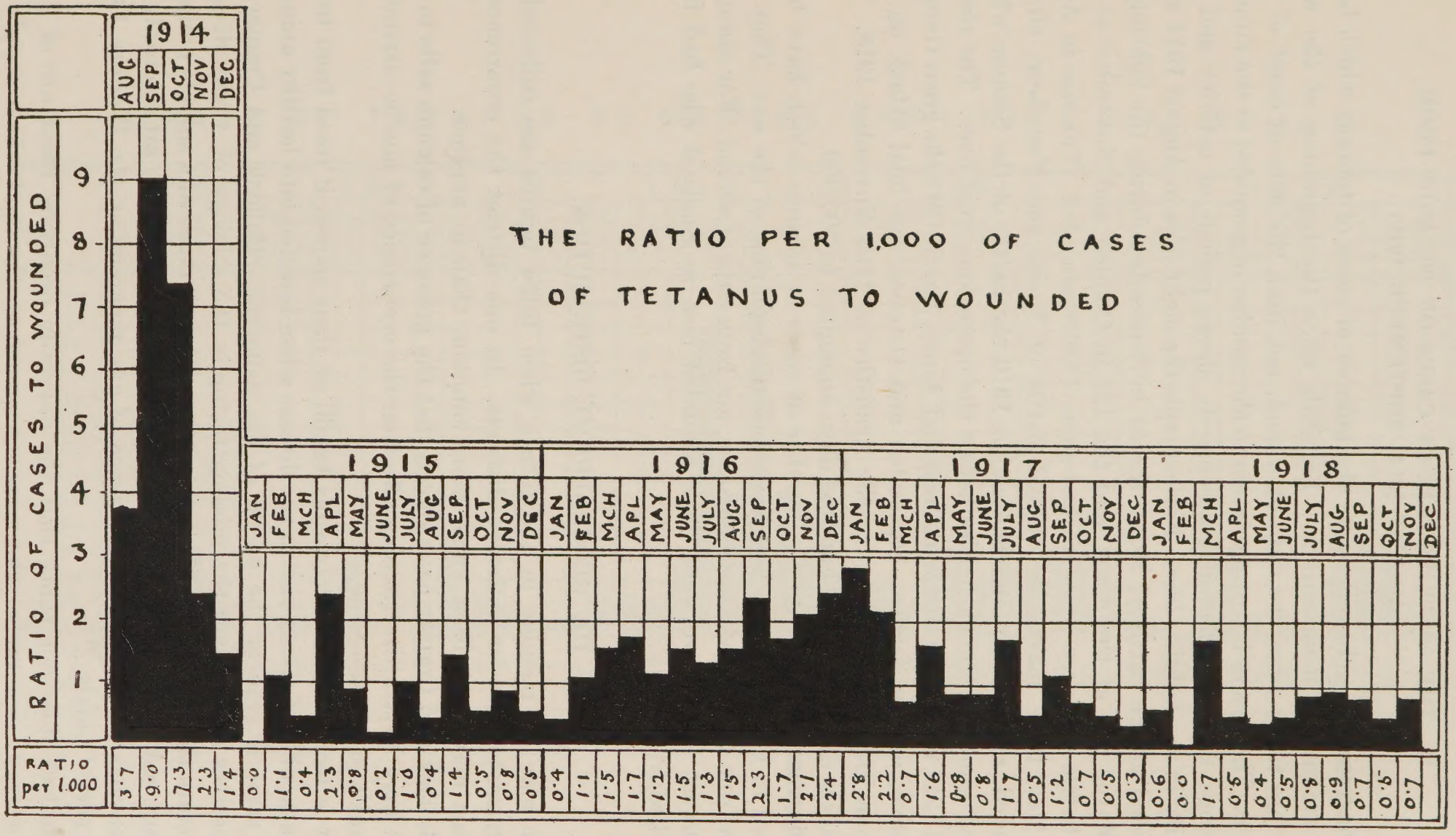


Diagram 1.

II. THE DISTRIBUTION OF CASES OF TETANUS FROM AUGUST 1914—SEPTEMBER 1918.

Diagram 2 merely represents the number of cases of tetanus which have been treated in home military hospitals since the beginning of the war. They are taken from the date of wound, not from the date of onset of the disease. The figures have no relation to the number of wounded or the number of troops engaged. The diagram merely shows periods of activity and inactivity in the fighting line. For example the eight men in August 1914 were wounded at the battle of Mons, the 54 in September during the fighting at the Marne and at the Aisne, and the 121 in October and November at the first battle of Ypres when we had some 13,000 wounded. The rise in April and May 1915, marks the second battle of Ypres and Festubert, 60,000 wounded, and in July and September 1916 the battle of the Somme which caused some 300,000 casualties before the operations were over. The rise in April 1917 marks the battle of Vimy and Arras; March 1918 the great German offensive, and in August, September and October, our final attack on the German lines which led up to the Armistice of 11th November 1918. The casualties during the last hundred days amounted to 300,000.

Diagram 3 represents the number of cases of tetanus which have been treated in home military hospitals since the beginning of the war. They are taken from the day of onset of disease, not from date of wound. For example, in August 1914 there were three wounded men in England who had been attacked by tetanus.

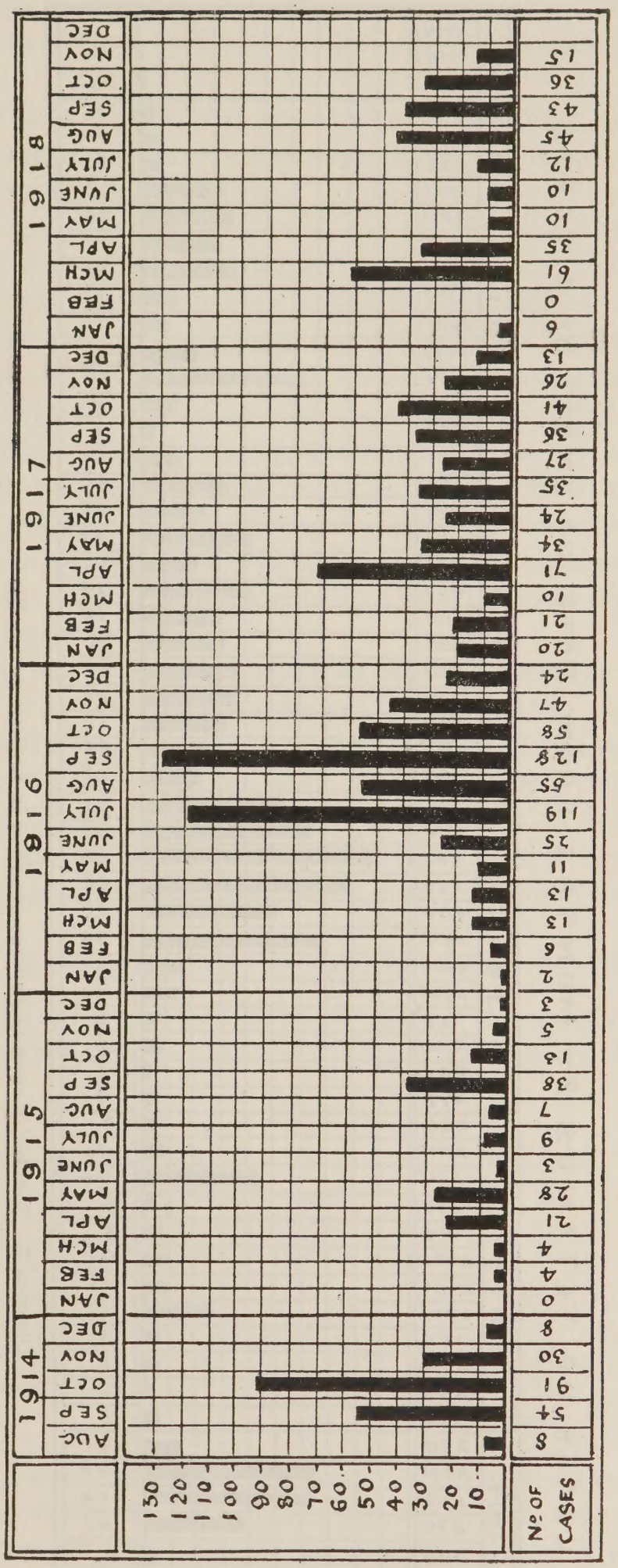
III. GEOGRAPHICAL DISTRIBUTION.

It may be possible in the future when fuller figures are collected to differentiate between different districts. In one district the occurrence of tetanus may have been much more common than in another.

Bullock and Cramer have shown that the presence of calcium salts in the earth may have a determining effect on the occurrence or non-occurrence of tetanus and gas gangrene.

It is well-known that tetanus bacilli or their spores, if freed from toxin, are incapable of giving rise to the disease when injected into healthy animals. The same is true of the bacilli of gas gangrene. Bullock and Cramer set themselves to discover the missing factor in the etiology of these diseases and state that they found it in injections of small doses of a soluble ionisable calcium salt. They state that these observations account satisfactorily for the curious fact that the occurrence of gas gangrene on the Western Front was very "patchy."

Bullock does not think that the naturally occurring rocks are of great importance; it is rather the manures spread on the land which supply the calcium salts which set in motion the tetanus and gas gangrene bacilli.


CASES OF TETANUS BY MONTHS FROM DATE OF WOUND.
1914
1915
1916
1917
1918
AUG SEP OCT NOV DEC JAN FEB MCH APL MAY JUNE JULY

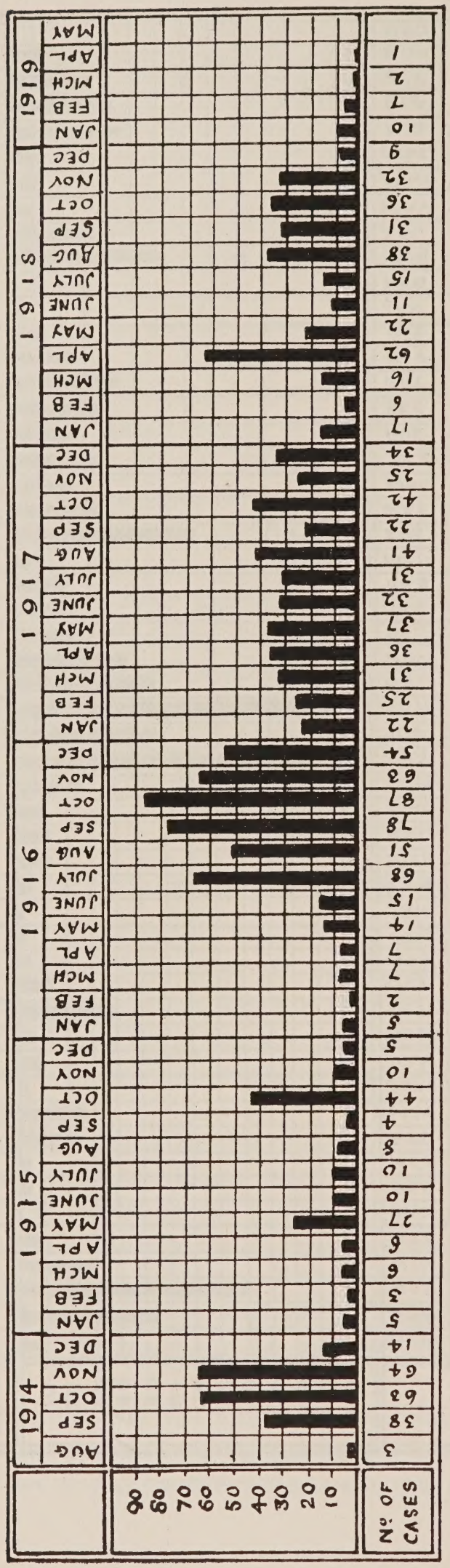


Diagram 3. Number of cases of Tetanus occurring in England during the war from date of onset.

After reading their paper an attempt was made to discover if any difference in the occurrence of cases of tetanus due to the geological formation could be made out.

To do this it is evident that the number of wounded, and the incidence of tetanus among them, occurring on a particular formation, for example the chalk, would require to be known.

This then could be compared with the incidence of tetanus among the same number of men wounded on another formation. For example, if in district A 100,000 wounded had an incidence of tetanus of 10 per 1000, and in district B the same number had only an incidence of 1 per 1000 a case would be made out. It might of course be due as Bullock thinks to district A being more intensively cultivated than the other, or it might be due to some chemical substance found in one formation and not in the other.

On consulting a geological map of the part of the Western Front held by the British it was seen that it all lay on a chalk formation covered over in patches by more recent gravels and sands. It seems therefore that it is very unlikely that any information on this subject would be gained by a comparative study of this front.

A spot-map was prepared showing as nearly as possible the position of wounded men who afterwards developed tetanus. After this was made it was evident that nothing could be gained from it. The information is not exact enough. Perhaps later on when more facts are available something might emerge. For the present it must be sufficient to draw attention to Bullock and Cramer's paper with the hope that further investigation may throw light on what promises to be a very interesting subject.

IV. CLASSIFICATION OF VARIOUS TYPES OF TETANUS.

The following table classifies as far as possible the cases of tetanus under four headings, as laid down in the third edition of the Memorandum on Tetanus.

Table I.

	Cases	Recovered	Died	Mortality per cent.
1. Trismus the *earliest* symptom				
(*a*) With complete closure of jaws developing within 24 hours after onset of symptoms	77	22	55	71·4
(*b*) With complete closure of jaws developing after 24 hours of onset	80	40	40	50·0
(*c*) With incomplete closure of jaws	505	380	125	24·9
2. Trismus occurring after other symptoms of tetanus have shown themselves	134	109	25	18·6
3. General tetanus without trismus	50	38	12	24·0
4. Local tetanus	201	201	—	0·0

Table I should be useful for prognosis. If trismus is the first symptom and is complete within 24 hours, the prognosis is bad, seven dying in ten; if the trismus occurs after other symptoms have declared themselves then only two die in ten.

As this classification has not been in use during the whole of the war, it has not been found possible to classify in this way all the 1458 cases under consideration. Many of the reports especially at the beginning of the war were sent in without any attempt at classification and at first cases of local tetanus either did not occur or were overlooked. These unclassified cases, 411 in number, were sent in simply with the diagnosis of tetanus, but as they occurred mostly at the beginning of the war and had a high rate of mortality it may be presumed that most of them were cases of general tetanus with trismus.

Table II represents the proportion of general to local tetanus as reported at different periods of the war.

Table II.

Type	Percentages				
	1914	1915	1916	1917	1918
General	98·9	98·6	87·0	76·6	83·5
Local ...	1·1	1·4	13·0	23·4	16·5

It is manifest that the ratio of cases of local tetanus to cases of general tetanus tended to become higher each year. This is due in part no doubt to the introduction of the prophylactic injection of antitoxin, also to an improvement in the diagnosis of mild and obscure cases of tetanus. What in the first years of the war would be considered to be due to a non-specific irritation of nerve and muscle, came afterwards to be recognised as a local manifestation of tetanus.

V. THE PERIOD OF INCUBATION.

(a) *At daily intervals.*

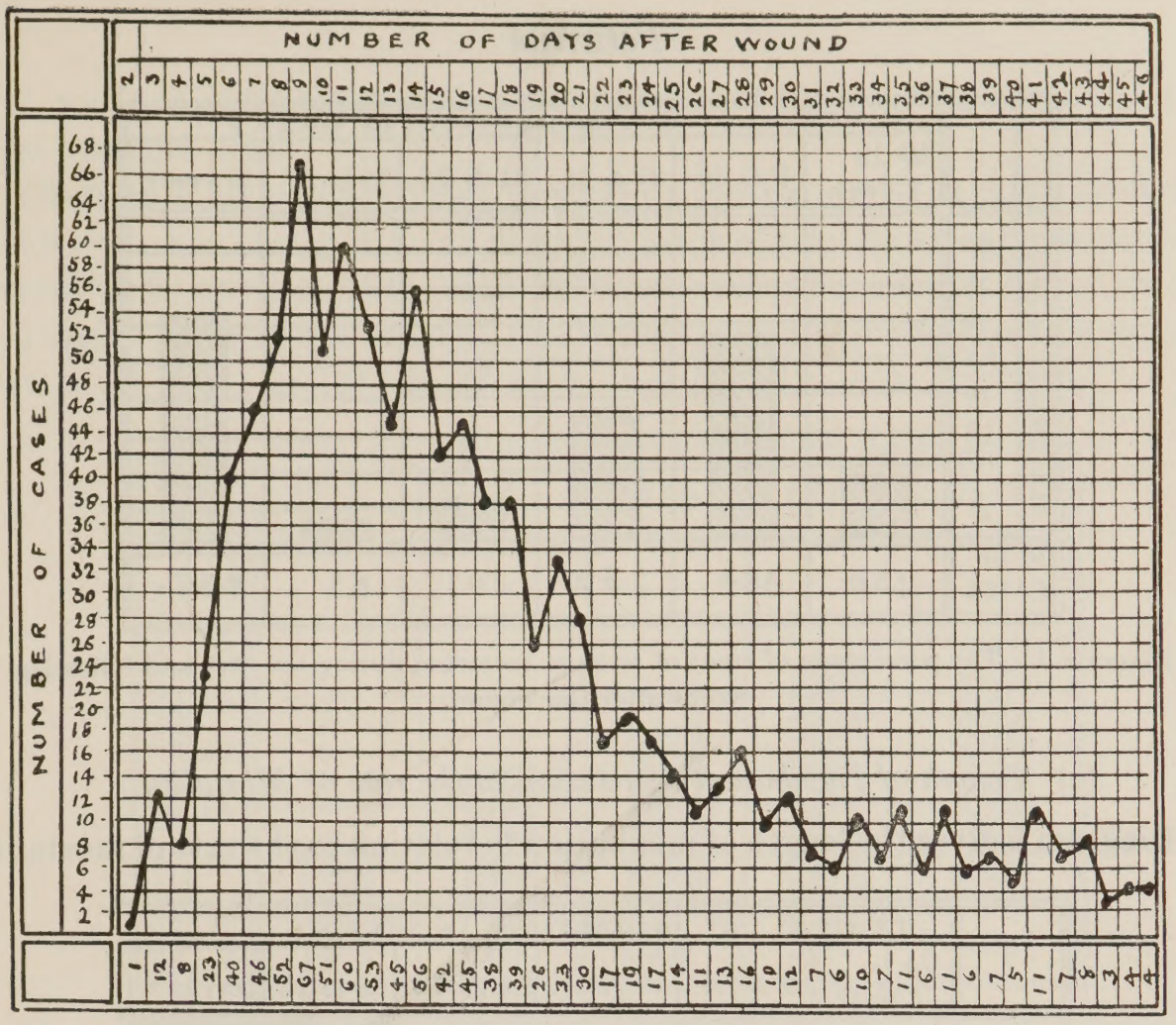
The incubation period, or the number of days which elapse between the date of wound, and the onset of tetanus symptoms, is represented by the following curve.

Curve A shows the number of cases which occurred on each day after the date of wound. The shortest period of incubation was two days, the longest two and a half years. The greatest number of cases occurred on the ninth day.

(b) *Periods of Incubation shown at weekly intervals.*

Diagram 4 gives the percentages of cases of tetanus occurring at weekly intervals.

From the above diagram it will be seen that in the 1458 cases under consideration, 9·5 per cent. of the cases are attacked during the first week; 28 per cent. during the second, and as many as 31·7 per cent. after five weeks. This diagram is very different from one made in pre-serum days, and as we shall afterwards see, is due to the prophylactic injection of antitoxin given soon after the wound is received.


NUMBER OF DAYS AFTER WOUND
NUMBER OF CASES
NUMBER OF DAYS AFTER WOUND (CONTINUED)
No OF CASES
NUMBER OF DAYS AFTER WOUND (CONTINUED)
No OF CASES
NUMBER OF DAYS AFTER WOUND (CONTINUED)
No OF CASES

Curve A.

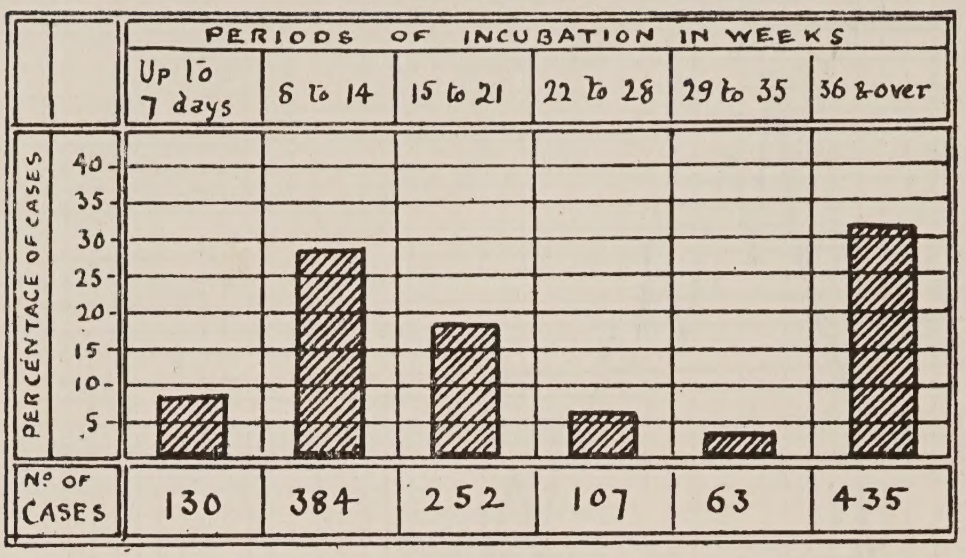


Diagram 4. The percentage of cases of tetanus occurring during the first and following weeks after the wound.

(c) *Length of Incubation in relation to the rate of Mortality.*

Diagram 5 gives the length of incubation in relation to the rate of mortality.

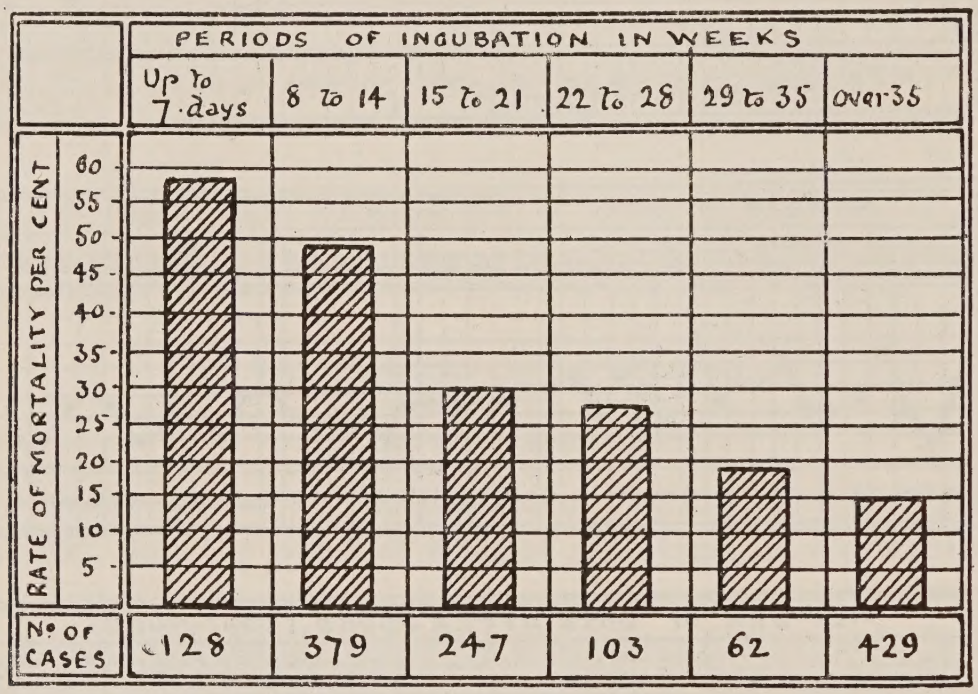


Diagram 5. Co-relation of the Rate of Mortality with the Length of Incubation.

From this diagram it will be seen that in 128 cases, with an incubation of seven days or under, the rate of mortality was 58·6 per cent.; in 429 cases with an incubation of more than 35 days, the mortality has fallen to 15·4. From this diagram it is abundantly plain that the shorter the period of incubation the higher the rate of mortality.

(d) *The variation in the period of incubation since the beginning of the war.*

This lengthening out of the period of incubation, which took place during the war, was undoubtedly mainly due to the introduction of prophylactic injections of antitetanic serum. Few wounded men received these in 1914

as it was not until the middle of October that the administration of anti-toxin had got under weigh.

Diagram 6 gives the average periods of incubation in days for each year of the war. For example, there were 138 cases of tetanus among the wounded treated in England in 1914; these had an average incubation period of only 11·8 days. In 1915 the average incubation period had risen to 27·3 days, in 1916 to 34 days; in 1917 to 48 days; and in 1918–19 to 50 days.

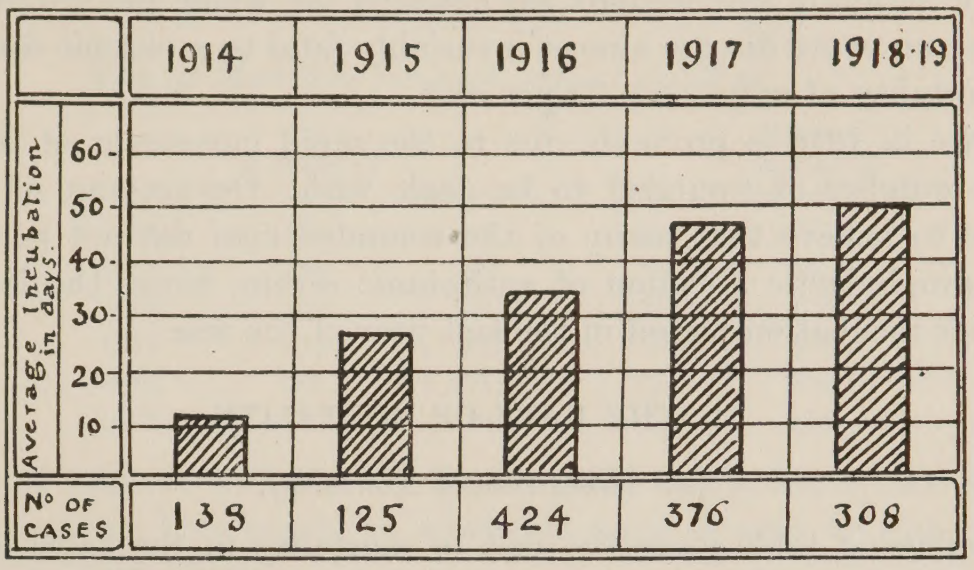


Diagram 6. The lengthening of the Period of Incubation since the beginning of the War.

In France the average period of incubation was much shorter. From July 1st to October 31st, 1916, there were 157 cases, with an average incubation of 12 days; from November 1st, 1916 to December 31st, 1917, 342 cases with an incubation of 13·2 days. This of course is due to the fact that the acute cases with a short incubation period would be treated in France; those with a longer incubation would have time to be transferred to England.

Table III gives the number, in percentages, of cases of tetanus with short, medium and long incubation periods which have occurred since the beginning of the war.

Table III.

Short, Medium, and Long Incubation periods since the Beginning of the War.

	Up to 10 days, per cent.	11 to 22 days, per cent.	More than 22 days, per cent.
1914	52·8	43·6	3·6
1915	29·9	40·8	29·9
1916	13·8	39·4	46·8
1917	15·2	26·8	58·0
1918	24·9	35·6	39·5

It will be seen that in 1914, 52·8 per cent. of the cases had a short incubation period of 10 days or under; this fell to 13·8 per cent. in 1916 and 15·2 per cent. in 1917. In 1918, however, it rose somewhat, about a quarter of the cases of tetanus in the last year of the war having a short incubation period. In

1914 there were only 3·6 per cent. of the cases with a long incubation period whereas this rose in 1917 to 58 per cent.

This is a remarkable result, and can be taken as a measure of the good effect of the prophylactic inoculation of antitetanic serum. During the first months of the war, as has already been pointed out, many of the wounded did not receive a primary injection, hence the number of acute cases with a short incubation. This introduction of the prophylactic inoculation of antitetanic serum in war wounds has changed the whole picture of tetanus, from being an acute disease almost invariably fatal to a chronic disease with a case mortality of only some 20 per cent.

The rise in 1918 is probably due to the rapid movement of troops and the large number of wounded to be dealt with. On account of this it is justifiable to believe that many of the wounded men did not receive their primary prophylactic injection of antitetanic serum, hence the lowering of the average incubation period in the last year of the war.

VI. THE RATE OF MORTALITY.

(a) *Gross rate of Mortality.*

The following table gives the rate of mortality in the cases of tetanus treated in home hospitals.

Table IV.

Rate of Mortality in cases of Tetanus occurring in England.

Number of cases	Recovered	Died	Rate of mortality per cent.
1437	936	501	34·8

Twenty-one cases are deducted from the 1458 as they undoubtedly died from other causes. It is therefore impossible to place them either among the recoveries or the deaths. The rate of mortality among cases of tetanus treated in England is 34·8 per cent. The cases in France have a higher rate since the severe acute cases with a short incubation would naturally be treated there. 715 cases up to the present have been reported from France; 510 of these died; a case mortality of 71·3 per cent. Combining the two sets of figures, there are 2152 cases and 1011 deaths; a rate of mortality of 47·0 per cent. The death rate in the pre-serum days lay about 85 per cent. This lowering of the death rate from 85 per cent. to 47·0 per cent. is doubtless due in great part to the introduction of the prophylactic inoculation of antitetanic serum. It would be much lower than 47·0 per cent. if only cases of wounded men who undoubtedly received a sufficient dose of antitoxin were taken into account. It must be remembered that, so far as prophylactic injections are concerned, we were still practically in the pre-serum days during the first months of the war. Further it is also true that during the whole of the war many cases escaped the preventive dose. Many cases of trench feet, for example, succumbed to tetanus before it was learnt that they must be treated as wounded men.

Doubtless also, owing to the exigencies of war service many wounded men would be marked up as having received a prophylactic injection, who did not in reality receive it.

(*b*) *The Rate of Mortality at different periods of the War.*

The number of cases of tetanus dealt with at different periods during the war and the rate of mortality are given in Table V.

Table V.

Rate of Mortality for each year of the War.

Years	Number of cases	Recovered	Died	Rate of mortality per cent.
1914	182	81	101	55·5
1915	138	60	78	56·5
1916	451	281	170	37·6
1917	376	294	76	20·5
1918	291	204	73	26·3
1919	20	16	3	15·0

From this table it will be seen that the fall in the death-rate has been fairly progressive. This result, to whatever cause it may be due, must be considered as satisfactory.

(*c*) *The position of the wounds in relation to the incidence and the mortality.*

There were 1458 cases of tetanus; 576 of these had multiple wounds and 882 single wounds.

Of the 576 multiple wounds, 392 recovered and 176 died; a case mortality of 31·0 per cent.

Of the 882 single wounds, 544 recovered, 325 died; a case mortality of 37·4 per cent.

There were 21 cases among the 1458 who died of other diseases. These are not included in the above figures.

The following table gives the position of the wounds in the 882 cases of single wounds.

Table VI.

Position of wound in cases of single Wounds.

Position	Number of cases	Incidence per cent.	Recovered	Died	Case mortality
Head, face and neck	29	3·3	24	5	17·2
Trunk	135	15·2	80	51	37·8
Upper extremities	236	26·7	132	101	43·3
Lower extremities	480	54·4	303	171	36·1

From this table it would appear that wounds of the lower extremity give rise to more cases of tetanus than wounds of other parts of the body, and it might be argued that this was due to the greater risk of earth contamination in these wounds. But to arrive at the truth in this matter it would be necessary

to know the ratio of wounds of the head to those of the other parts. This varies in different wars. What it is in this war has not yet been calculated. In the old wars the average ratio was given as 12, 19, 27 and 42. That is to say there were admitted to hospital 12 cases of head wound, 19 of trunk, 27 of the upper extremities and 42 of the lower extremities for every hundred cases treated.

(*d*) *The effect of Fractures on the rate of mortality in cases of Tetanus.*

Table VII.

Wound	Number of cases	Recovered	Died	Mortality per cent.
Fracture ...	492	349	143	29·1
No fracture...	945	587	358	37·9

Twenty-one died of other causes, there were among them nine fractures.

It has been stated that the presence of a fractured bone in a wound raises the death-rate in cases of tetanus. From the above figures it will be seen that the advantage on the contrary lies with the fractures. It can be readily imagined that the addition of a fracture to a wound might increase the incidence of the disease among wounded men. It is more difficult to understand why the complication of a fracture should heighten the rate of mortality. In regard to the relation of fractures to incidence it is impossible at present to make any statement as the figures are not available.

In the former a fracture should increase the liability of the wounded man to take tetanus, but when once tetanus has supervened it should make little or no difference in the risk whether he has a fracture or not.

(*e*) *Tetanus occurring after operative interference with the wound.*

Table VIII.

Number of cases	Recovered	Died	Case mortality per cent.
102	67	35	24·5

Among the 1458 cases, 102 are reported to have supervened after a surgical operation. There were 35 deaths, a case mortality of 24·5 per cent.

The Tetanus Committee recommended that when operations are performed, at the site of wounds, even if they are healed, a prophylactic injection of serum should always be given. Among these 102 cases only 7 are stated to have received this prophylactic inoculation before the operation. All seven recovered. There is no record of the effect of prophylactic injections before operation on the incidence of the disease. Only those cases of operation which resulted in tetanus are given. The small number of cases recorded as having received an injection before an operation, would almost go to show that most of those who received the injection did not develop symptoms of tetanus. It has been shown that tetanus bacilli may lie latent for years at the site

of wounds; a prophylactic injection of antitetanic serum before operation would therefore appear to be a reasonable precaution.

Among the cases of tetanus there were some curious examples, which it may be of some interest to record.

	No. of cases	Recovered	Died
Appendicitis	5	2	3
Vaccination	2	1	1
Haemorrhoids	2	1	1
Inguinal hernia	1	—	1
Varicocele	1	—	1
Blister, pricked with dirty needle ...	1	1	—
No wound discovered	2	2	—
Ulcer of scrotum	1	—	1
A fish-bone stuck in finger while working in garden where fish-manure had been used	1	1	—
Prick of a thistle	1	1	—
Trench feet and frost bite...	38	20	18 (47·3)
Trench feet before 1917	20	5	15 (75)
Trench feet after 1917	18	15	3 (16·6)

At first trench feet were not treated as wounds and no prophylactic serum was given until the resulting death-rate of 75 per cent. Afterwards when serum was given the rate fell to 16·6 per cent.

(*f*) *On operative interference after tetanus symptoms have appeared.*

Table IX.

Number of cases	Recovered	Died	Mortality per cent.
74	56	18	24·3

The opinion of the Tetanus Committee was that it appeared safer to abstain from surgical interference with a wound after tetanus had appeared. In the 1458 cases, there were 74 which had had such an operation. Of these 56 recovered and 18 died, a case mortality of 24·3 per cent. From this it would appear that operative interference after tetanus symptoms have declared themselves, is not the dangerous procedure it has been supposed to be.

If tetanus symptoms supervene on a wound it would appear to be the best course for the welfare of the patient to thoroughly cleanse the wound and remove any sequestra or scar tissues which may be harbouring the bacillus. But if an operation is decided on it would be well to see that the tissues are well flooded with antitoxin, lest the interference with the wound may let loose on raw surfaces a further quantity of toxin.

(*g*) *Relation of the Rate of Mortality to the number of days which elapse between the date of wound and the onset of symptoms.*

Diagram 7 shows that in the 1458 cases dealt with in home military hospitals, if the symptoms of tetanus appeared within ten days of receiving the wound, the rate of mortality was 58·1 per cent., if from the eleventh to

the twenty-second day, 35·3 per cent. The remaining 579 cases with an incubation period of more than twenty-two days, 17·3 per cent. This is the

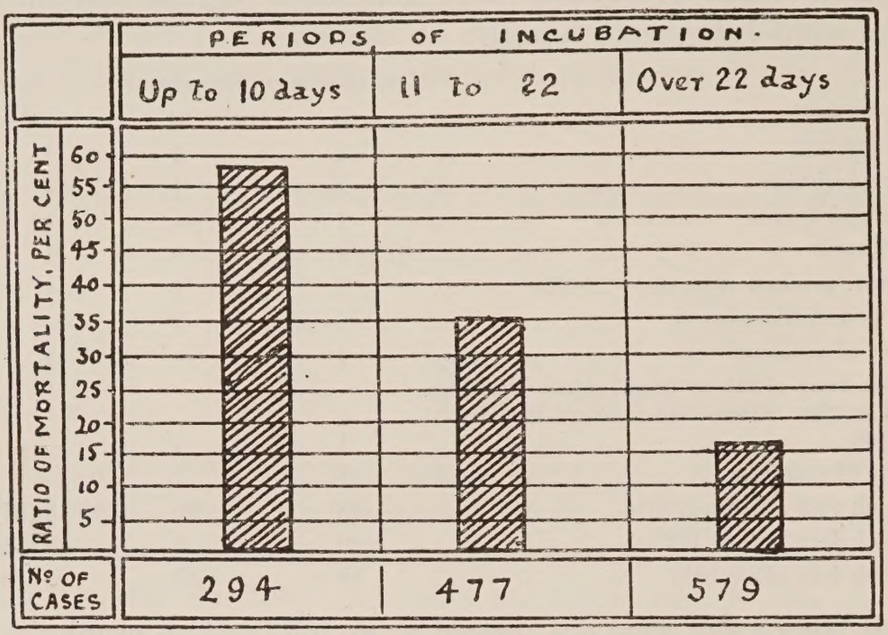


Diagram 7. Death Rate in Cases of Tetanus with short, medium and long Periods of Incubation.

old story; the longer the period of incubation, the lower the rate of mortality. In eighty-seven cases the period of incubation could not be calculated on account of a lack of information in the reports.

VII. PROPHYLACTIC OR PREVENTIVE TREATMENT OF TETANUS.

The anticipation and prevention of tetanus, as in so many other diseases, is by far the most important means of defence. In the first line we may place the proposed league of nations. If there were no wars men would not be called on to stand up to the knees in filthy mud and be torn and lacerated by rough and dirty pieces of shell. It seems a strange and barbarous thing to do, and it is to be hoped that in the course of evolution, mankind will become sufficiently intelligent to find some other way of settling his differences. At the present time, however, it is necessary to find other methods of prevention as man has not yet sufficiently emerged from the savage.

Given then war, and the conditions of warfare which prevailed during the great war, we must expect tetanus to supervene in a certain proportion of the wounded. In the South African war there was little or no tetanus. The wounds were mostly caused by bullets and the veldt was clean. In France the soil was heavily manured and the wounds were largely caused by shell-fire.

The next most important line of defence is the surgical treatment of the wound. This has already been alluded to in the section on the incidence of cases among the wounded. The surgeon's knife, after all is said and done,

is the best means of preventing the occurrence of tetanus after the wound has been inflicted. Dead putrifying tissues is the best culture medium for the anaerobe. At the beginning of the war the treatment of wounds was not thorough enough at the primary operation. It was thought sufficient to wash out the wound and apply an antiseptic. Controversy was acute in regard to the merits of chlorine, common salt, bipp, flavine, etc. It was only when surgical teams were boldly pushed up to the front, and thorough excision of the damaged tissues in the wounds carried out, with primary or primary delayed suture, that any real advance was made in treatment. Anyone who saw these wounds in the base hospitals in France a few days after they had been inflicted, must have been struck by the extraordinary results. One could almost foresee the time when antitetanic serum would no longer be required.

Major Gibson may be quoted in this connexion. "The early incision of wounds began about the middle of 1917, and beyond the very remarkable drop in the incidence of tetanus, due to prophylactic injection, the practice of general excision had a further effect on the incidence of the disease. From 103 per 100,000 in the pre-incision days, the rate of tetanus had fallen to 24 per 100,000 in February 1918. In May there were only 12 cases per 100,000 and 8 per 100,000 in June."

Next in importance as a preventive measure is the prophylactic injection of antitetanic serum. This war has shown that the prophylactic value of antitoxin is beyond all doubt. The first thing in this connexion to be discussed is:—

(*a*) *The Incidence of Tetanus among protected and unprotected wounded soldiers.*

Some two months after the beginning of the war it was ordered that every wounded man should receive an injection of 500 units of antitetanic serum as soon after he was wounded as possible. That this had a most important influence on the incidence of tetanus among the wounded men is amply proved by Diagram 1. In that diagram it is shown that the ratio of the number of cases of tetanus to the number of wounded was several times as high in September and October as in November and December. In September it was 9 per 1000, in December it fell to 1·4 per 1000. Now this fall was undoubtedly due to the fact that few prophylactic inoculations of antitetanic serum were made until the middle of October. It appears that only a small quantity of the serum was taken out with the Expeditionary Force in August 1914, and this only for purposes of treatment. It was not until the number of cases of tetanus became alarming that steps were taken to secure a large supply and ensure that every wounded man received a prophylactic dose. It was not until about the middle of October that prophylactic inoculation was introduced on anything like an adequate scale, and it was at this time that the remarkable fall in the incidence of the disease took place.

(*b*) *The Incubation period in non-protected and protected cases.*

The next question is, what effect has the prophylactic inoculation on the length of the incubation period? The following diagram represents the incubation period in the protected and the unprotected. There are 899 protected and 213 unprotected among the 1458. Many cases are not recorded.

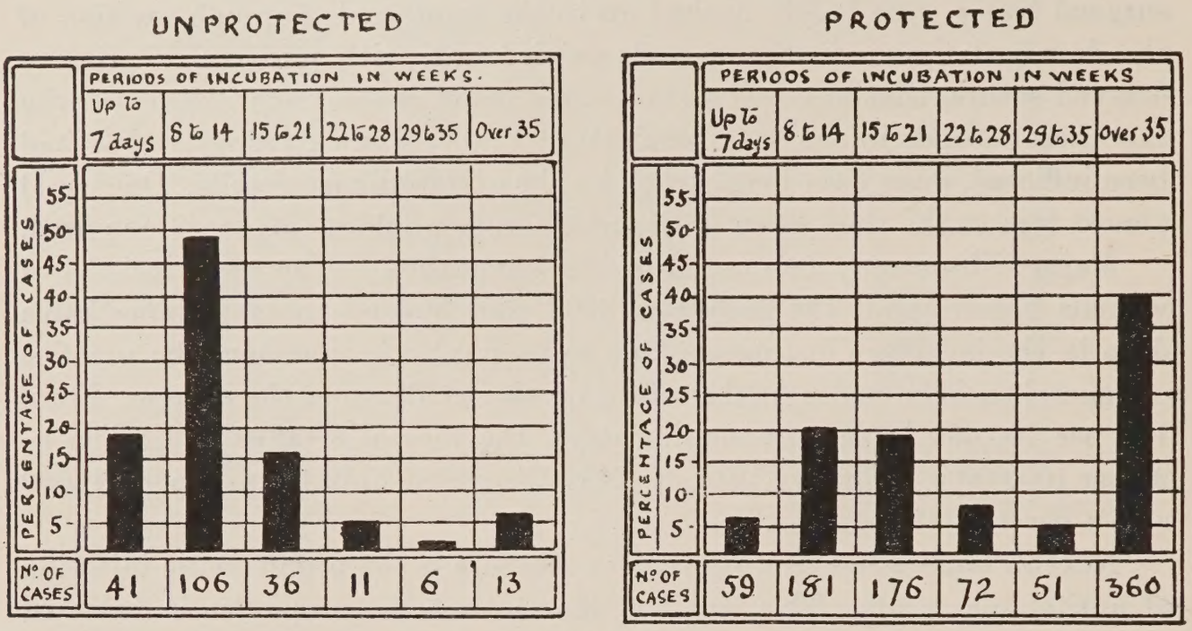


Diagram 8. Comparison of the Period of Incubation in Protected and Unprotected.

Diagram 8 shows that the incubation period is much lengthened in the protected. Only 26·9 per cent. of the protected are attacked by tetanus during the first fortnight, whereas 68·9 of the unprotected are attacked in the same period. Forty per cent. of the protected have an incubation period of more than 35 days, only 6·5 per cent. among the unprotected.

Taking all the cases the average incubation among the protected is 45·5 days, among the unprotected 10·9 days.

It is therefore abundantly manifest that the prophylactic injection of antitoxin lengthens in a marked degree the length of the period of incubation.

(*c*) *The Rate of Mortality among the protected and the unprotected.*

The following table gives the figures:—

Table X.

Comparison of the Rate of Mortality in the Protected and Unprotected.

	Number of cases	Recovered	Died	Rate of mortality per cent.
Protected	899	676	203	22·5
Unprotected and Unrecorded	559	260	298	53·3

Among the 1458 cases under consideration 899 (61 per cent.) are noted as having received a prophylactic injection of antitetanic serum. Of these

899 protected cases, 676 recovered and 203 died, giving a mortality of 22·5 per cent. In the remaining 559 cases there is no record of prophylactic treatment, although in all probability many of them received it. Of these 260 recovered and 298 died, a mortality of 53·3 per cent.

These figures go to show that the prophylactic inoculation of antitoxin lowers the mortality more than one-half, namely from 53·3 per cent. to 22·5 per cent. Further it must be borne in mind that many wounded men came over from France, especially during the first half of the war, without any records. There was no Field Medical Card at that time. These unrecorded cases have been placed among the unprotected class.

(*d*) *The effect of multiple prophylactic inoculations on the incidence of tetanus among the wounded.*

At the beginning of the war one prophylactic inoculation was the rule, but in June 1917, it was ordered that four should be given at intervals of seven days, each injection to consist of 500 units. If multiple inoculations are more useful than a single dose, this should show itself in a lowered incidence of tetanus among the wounded. At present it is impossible to make any statement as the data available are insufficient. It is true that the incidence in the latter half of 1917 is lower than in the corresponding part of 1916, as shown in Diagram 1, but whether this is in any way due to the introduction of multiple doses or not it is difficult to say. When all the figures are available it may be possible to see the effect.

Col. Lingard, R.A.M.C., Queen Mary's Military Hospital, Whalley (Lancs.), gives some interesting details bearing on this question. He states that since the order was issued on 17th June 1917, and had time to be introduced and carried into effect, 15,152 surgical patients of the British Expeditionary Force have been admitted to this hospital, without a single case of tetanus developing. He considers this a most encouraging and satisfactory result and that it justifies all the extra expense and labour involved in the multiple inoculations.

At present then the question must be left without a definite answer. One argument in favour of multiple prophylactic inoculations is that if the wounded man has escaped the primary dose owing to the stress of war, this is made good seven days afterwards.

(*e*) *The effect of one or more than one inoculation on the incubation period.*

Diagram 9 gives the number of prophylactic inoculations, the number of cases and the average incubation in days. With one inoculation, the average incubation is 38·2 days; with two, 33·6 days; with three, 51 days; and with four or more 83·7 days.

From this it would appear that the incubation period tends to lengthen as the number of inoculations increases; but whether this is due to the multiple injections or not, it is difficult to say.

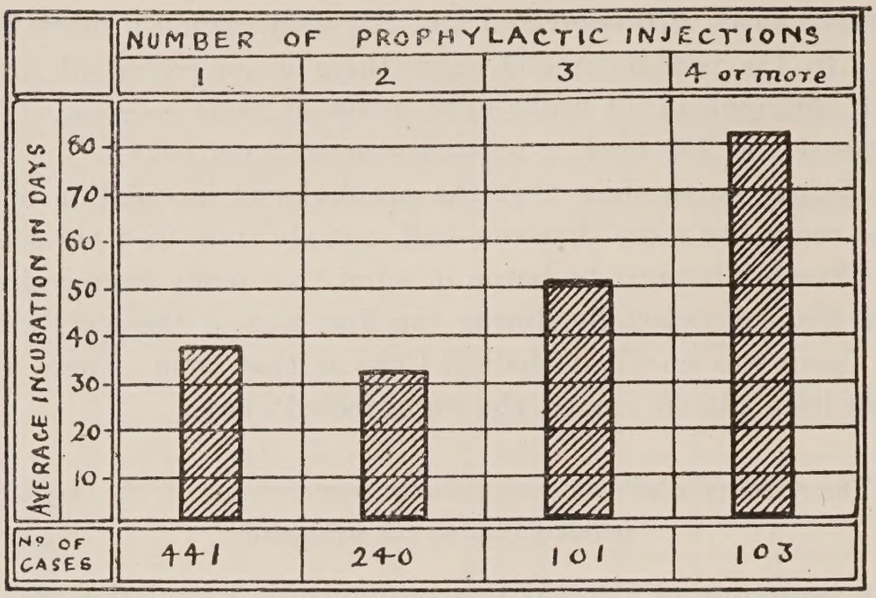


Diagram 9.

(*f*) *On the effect of one, or more than one, prophylactic inoculation on the rate of Mortality.*

Diagram 10 represents the effect of one, or more than one, prophylactic inoculation on the death-rate. From it will be seen that wounded men who received one inoculation had a case mortality of 25·1 per cent.; those who received two, 21·3 per cent.; three, 16·5 per cent.; and four or more 7·1 per cent.

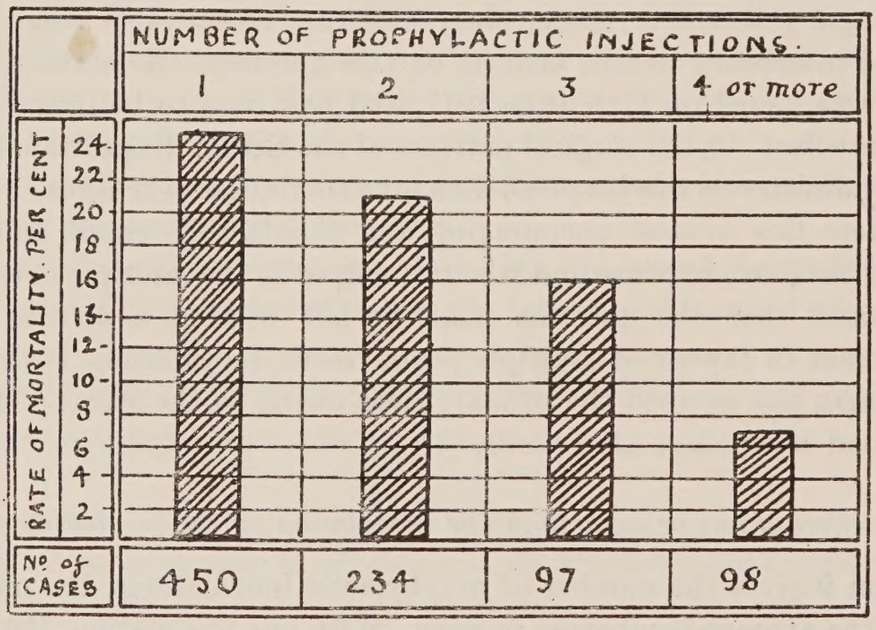


Diagram 10. The effect of one or more prophylactic inoculations on the death-rate.

From these diagrams it may be said that the Tetanus Committee were justified in recommending multiple prophylactic injections. The incubation period appears to be lengthened and the death-rate diminished. Whether this is really due to the increase in the number of inoculations, or merely to

the fact that the cases which receive three or four injections are naturally the milder, more chronic, slower cases of the disease, with a lower rate of mortality, it is impossible to say. But although it must be confessed that the value of this procedure is by no means proved by these figures, it will probably be safe to recommend that multiple inoculations should be continued until more evidence is accumulated.

(*g*) *What effect, if any, has the time of inoculation on the rate of mortality?*

In regard to what influence promptitude in giving the prophylactic inoculations has on the rate of mortality, the following table gives all the information available from the 1458 cases.

Table XI.

The effect of the time of inoculation on the rate of Mortality.

Number of cases	Prophylactic inoculation	Recovered	Died	Mortality per cent.
611	On day of wound	467	144	23·5
140	One day after wound	111	29	20·7
106	Two days after wound	79	27	25·4

From this table it would appear that it is better to be inoculated the day after receiving the wound than on the day of the wound. But after all there is not much difference in the three rates and it probably does not make much difference in the death-rate whether the first prophylactic inoculation is given on the day of wound or a day or two after. At least this is what the figures would seem to show. There probably is some effect on the incidence of the disease among the wounded, and it would appear to be self-evident that the sooner the prophylactic is given after the wound is received, the better.

(*h*) *On the results obtained from the Increase of the Primary Prophylactic dose from* 500 *to* 1500 *units.*

On the recommendation of the Adviser in Pathology to the British Expeditionary Force in France, the primary prophylactic dose was changed from 500 to 1500 units. This change took place about the beginning of August 1918. The following table shows the amount of the primary prophylactic dose, the number of cases, the average period of incubation, and the rate of mortality.

Table XII.

The effect on the rate of Mortality of the amount of the primary dose of serum.

Primary prophylactic dose	Number of cases	Average length of incubation in days	Rate of mortality per cent.
500 units	238	38·6	22·4
750 ,,	140	42·1	16·4
1000 ,,	40	59·0	10·5
1500 ,,	106	25·0	27·4

This table is given for what it is worth. From it will be seen that 238 cases of tetanus which received a primary prophylactic dose of 500 units had an incubation period of 38·6 days and a death-rate of 22·4 per cent.; whereas 106 men who are stated to have received a primary dose of 1500 units had an incubation period of only 25 days and a death-rate of 27·4. The deduction is that the primary injection of 500 units as recommended by the Tetanus Committee, should be continued, as it seemed to be quite as efficacious as the 1500 units. This will mean economy, in money, space and transport. Further it is probable that 3 c.c. of horse serum are better borne and give rise to less irritation than 9 c.c.

It must also be remembered that four prophylactic doses are given at intervals of seven days. If only one dose is given it is possible that a larger primary dose than 500 units might be given with advantage, but there is no proof of this.

(*i*) *The addition to the antitetanic serum of the antitoxins of other anaerobes found in wounds.*

It may be useful to record here that attempts were made towards the end of the war, to add to the antitetanic serum the antitoxins of *B. welchii*, *Vibrion septique* and *B. oedematiens*. An account of this is given in the fourth edition of the Memorandum on Tetanus and also in *War Medicine*, December 1918.

It will be sufficient to say here that no satisfactory or practical results came of these attempts, as the war ended before the methods were at all perfected. If this attempt is made at any future time it would be advisable to make the experiment independently of the antitetanic serum lest the latter be brought into disrepute and we lose the substance in snatching at the shadow.

VIII. THERAPEUTIC OR CURATIVE TREATMENT OF TETANUS.

This is undoubtedly a difficult subject to be dogmatic upon. The curative treatment of tetanus by carbolic acid, magnesium sulphate and other salts may be dismissed with the remark that in home hospitals they proved a failure and soon dropped out of the running. The only specific therapeutic treatment is by the injection of tetanus antitoxin. It has been proved up to the hilt that the prophylactic inoculation of antitoxin is of very great value; lowering the incidence, lengthening the period of incubation and lessening the death-rate. But when an attempt is made to appraise the value of antitoxin, given after the symptoms of tetanus have declared themselves, great difficulty is met with. Wide differences of opinion are held, many holding that if given early and in sufficient quantity it acts powerfully for good; others doubting its usefulness but hesitating to discard it altogether. The latter argue that as it is the only rational specific drug against tetanus in

our possession it would be wrong to withhold it in such a fatal disease as tetanus. They think there is an off chance that it may turn the scale in favour of the wounded man.

The experimental evidence is in favour of the antitoxin as a curative agent. Prof. Sherrington has shown that serum treatment of experimental tetanus in monkeys shows a recovery rate in a series of 25 animals of 44 per cent. The monkeys were inoculated with a dose of tetanus toxin more than eight times the minimum lethal dose. The antitetanic serum was not brought into play until twelve to sixty hours after the symptoms of tetanus had declared themselves. It is true that there is a great difference in tetanus in man and experimental tetanus in the monkey. In the one case there is present the living tetanus bacillus, in the other a weighed quantity of the dead poison. But the fact still remains that here we have animals, suffering from definite symptoms of tetanus, who would undoubtedly all die in a very short time if untreated, receiving a single dose of antitoxin with the result that half of them recover.

In regard to the statistical proof of the value of antitoxin as a curative agent, it is doubtful if any truth can be arrived at by the study of the figures at our disposal. There is no uniformity in the treatment of tetanus in man. The men who suffer are also, as a rule, suffering from other grievous maladies—wounds, fractures, septicaemias, pneumonias, haemorrhages, heart failures, etc., so that if the man dies it is impossible in many cases properly to fix the blame.

Capt. Golla, a member of the Tetanus Committee, has compared the results obtained from the use of therapeutic serum in this war with those of pre-serum days. He is of opinion that the rate of mortality in cases of tetanus in this war which did not receive a prophylactic injection of antitoxin but did receive therapeutic treatment, approaches very closely to the rate of mortality in pre-serum days. In other words, it would appear from his figures that the therapeutic use of serum is of little or no practical value in treatment. It is taught at the present time that tetanus toxin which has been taken up and fixed by the nerves or nerve cells is inaccessible to antitoxin. If a lethal dose has been taken up by the nerves and is travelling towards the nervous centres, before the serum treatment is begun, then no amount of antitoxin will save the patient.

But in spite of these statistical considerations, and in view of the experimental results, it is clear that medical officers will continue for the present to give a case of tetanus the benefit of the doubt and use antitetanic serum therapeutically. As Ransom states, it may neutralise some of the free toxin in the blood and lymph, and prevent it ultimately entering the nervous system and causing death, when the toxin already admitted through the motor nerves is not sufficient to do so.

It remains then to decide as to the best route and the best dosage.

The total quantity of antitetanic serum issued to the army during the

war was 11,258,125 doses of 500 units of low potency serum and 27,549 doses of 8000 units of high potency serum.

(*a*) *What is the best route for the administration of antitetanic Serum?*

No answer to this question can be given from a study of the figures available for this report. Experience during the war does not seem to have led to any uniformity of practice. In one school a large single dose of some 30,000 units of antitoxin given intravenously is the method used. In another the subcutaneous route is chosen, and as much as 100,000 units given during the first 24 hours. In yet a third the intramuscular is considered the best. The Tetanus Committee on the other hand are of opinion that in acute general tetanus the best method of treatment lies in the earliest possible administration of large doses of antitetanic serum by the intrathecal route. The Committee agrees that the intravenous route is an excellent and rapid method of giving serum, but thinks that the danger from anaphylactic shock renders it less useful.

As there did not seem to be any hope of proving which is the best route from the figures at their disposal the Committee instituted a series of animal experiments. Prof. Sherrington carried these out at Oxford, and the result is given in the following table.

Table XIII.

On the effect of route on the administration of antitetanic serum.

Route	Number of animals used	Number of deaths	Number of recoveries
Subcutaneous ...	25	23	2
Intramuscular ...	25	22	3
Intravenous ...	25	18	7
Lumbar subdural	25	11	14
Bulbar subdural	20	7	13
Cerebral subdural	10	10	—

It will be seen from the above table that the results are indubitably in favour of the intrathecal route.

Out of the total of 1458 cases of tetanus treated in home hospitals, 1389 had injections of antitetanic serum after the onset of the symptoms. Of these 923 recovered and 466 died, a rate of mortality of 33·5 per cent.

The following table gives the various routes employed in the administration of antitetanic serum in the 1389 cases. In the remaining 69, 43 had no therapeutic injection of any kind, 21 died of other diseases and in 5 the route is not specified. This tabular statement is given in order to place on record the methods used during the war. It is useless for the purpose of obtaining evidence as to the best route.

Table XIV.

Cases were treated by injections of serum	Cases	Recovered	Died	Mortality per cent.
Subcutaneous alone	248	129	119	47·9
Intramuscular alone	133	119	14	10·0
Intravenous alone	33	16	17	51·5
Intrathecal alone	43	19	24	56·5
Subcutaneous and intramuscular	85	76	9	10·6
Subcutaneous and intravenous	49	23	26	53·0
Subcutaneous and intrathecal ...	163	88	75	46·0
Intramuscular and intravenous	28	18	10	35·7
Intramuscular and intrathecal	250	177	73	29·2
Intravenous and intrathecal ...	24	11	13	54·1
Subcutaneous, intramuscular and intravenous	9	3	6	66·6
Subcutaneous, intramuscular and intrathecal	205	161	44	21·4
Subcutaneous, intravenous and intrathecal	45	31	14	31·1
Intramuscular, intravenous and intrathecal	47	30	17	36·1
Subcutaneous, intramuscular, Intravenous and intrathecal	27	22	5	18·5

(b) What is the best dosage.

The Tetanus Committee recommended in their Memorandum that in the treatment of acute general tetanus large doses should be given. The term "large dose" is not very definite. By it the Committee meant about 24,000 units in 24 hours. Towards the end of the war a circular was sent round by the British Medical Authorities in France recommending much larger doses. The circular states that the treatment of generalised tetanus by means of antitoxin had not so far given encouraging results, and that in a recent series of 60 cases the case mortality was 71·2 per cent. The dosage of 24,000 units on the first days, as recommended by the Tetanus Committee, was looked upon as too small, and a dosage three times as large was advocated. Three cases are reported in which recovery took place after very large doses. The first received 64,000 units during the first 24 hours, given in three intrathecal, one intravenous and four subcutaneous injections. Eight different injections in the first 24 hours and all of 8,000 units. This may be necessary, but it is difficult to picture such a quantity of toxin circulating in the blood and lymph as to require such a huge quantity of antitoxin for its neutralisation. The first two cases are reported to have had severe serum rashes, and one is reported to have had a moderate anaphylactic shock. It surely cannot be necessary to give such large and numerous doses. If symptoms of tetanus appear it seems necessary with our present knowledge to inject antitoxin. Animal experiments show that the intrathecal route is the most efficacious. One would therefore conclude that a dose of 20 c.c. of high potency serum, containing 16,000 units, given intrathecally on the first and second days, supplemented and continued by intramuscular and subcutaneous injections

would be sufficient to keep the fluids of the body amply supplied with antitoxin.

In regard to the quantities of antitoxin used therapeutically in home hospitals during the war the following two tables give approximately the total amount of serum given, and the average daily amount.

Table XV.

The Total quantity of antitoxin given in Home Military Hospitals.

Out of the 1381 cases				Recovered	Died	Mortality per cent.
15	received	1,000 units or under		7	8	53·3
156	„	1,001 „ 5,000	„	79	77	49·3
144	„	5,001 „ 10,000	„	64	80	55·5
106	„	10,001 „ 15,000	„	65	41	39·6
84	„	15,001 „ 20,000	„	49	35	41·6
166	„	20,001 „ 30,000	„	104	62	37·3
114	„	30,001 „ 40,000	„	84	30	28·0
180	„	40,001 „ 60,000	„	123	57	31·6
202	„	60,001 „ 100,000	„	155	47	23·1
158	„	100,001 „ 200,000	„	141	17	10·7
32	„	200,001 „ 300,000	„	26	6	18·7
9	„	300,001 „ 400,000	„	8	1	11·1
9	„	400,001 „ 500,000	„	9	—	—
4	„	500,001 „ 600,000	„	4	—	—
2	„	600,001 „ 900,000	„	2	—	—

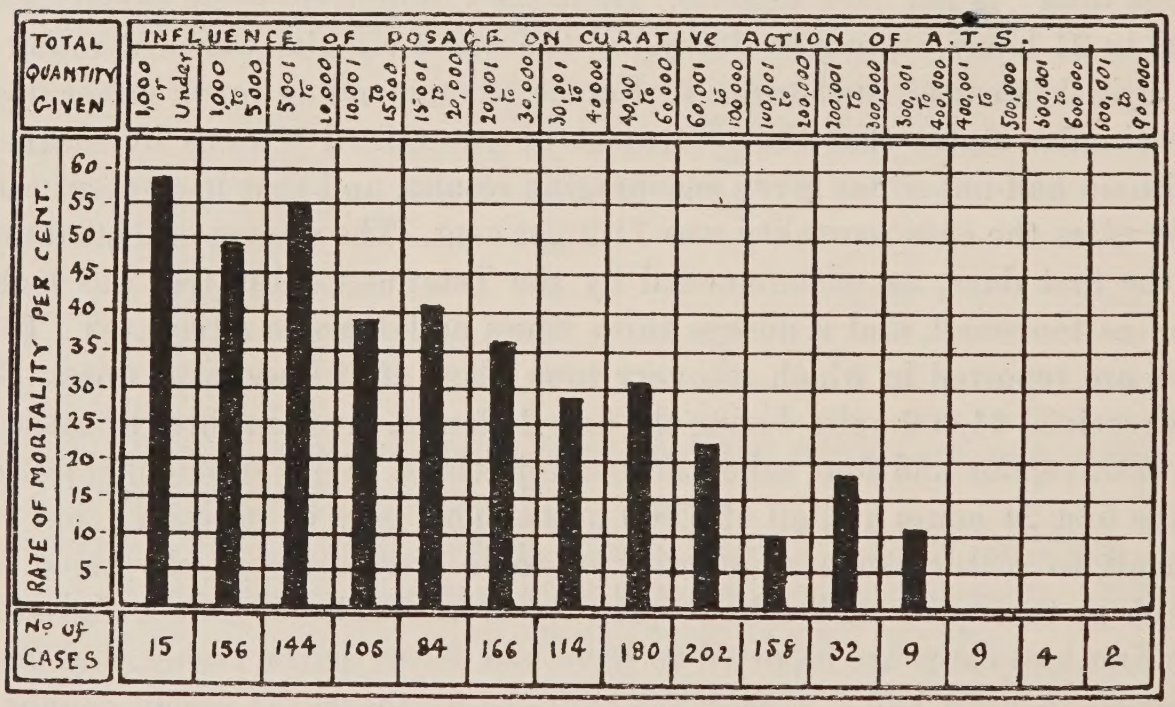


Diagram 11. Influence of dosage on curative action of antitoxin.

It appears from **Diagram 11** that the greater the amount of serum given the lower the mortality. This probably merely means that the longer the man lived the more serum he received. The short acute cases died before they had time to receive a large quantity. Some of the men received very large quantities indeed. One man for example received 150,000 units daily for

3 days; an average of 45,000 for 20 days; the grand total being 900,000 units. If ordinary serum was used at 1500 units to 10 c.c., then the man received 6 litres of horse serum in 20 days. As each dose of 500 units costs one shilling then this man's treatment cost £90 in serum alone. This huge quantity was all given intramuscularly; the man is reported to have had a slight serum rash, and that he recovered.

Table XVI.

The average daily quantity of antitoxin given during the attack.

Out of the 1381 cases					Recovered	Died	Mortality per cent.
36	received	1,000	units or under		24	12	33·3
487	,,	1,001 ,,	5,000	,,	308	179	36·1
363	,,	5,001 ,,	10,000	,,	280	83	22·8
194	,,	10,001 ,,	15,000	,,	145	49	25·2
114	,,	15,001 ,,	20,000	,,	78	36	31·5
109	,,	20,001 ,,	30,000	,,	48	61	55·9
47	,,	30,001 ,,	40,000	,,	23	24	57·0
25	,,	40,001 ,,	60,000	,,	11	14	56·0
6	,,	60,001 ,,	100,000	,,	3	3	50·0

Diagram 12 gives the average daily dose. Here an opposite condition prevails. The larger the dose the higher the mortality. This probably merely means that the more severe cases received larger daily doses than the less severe cases.

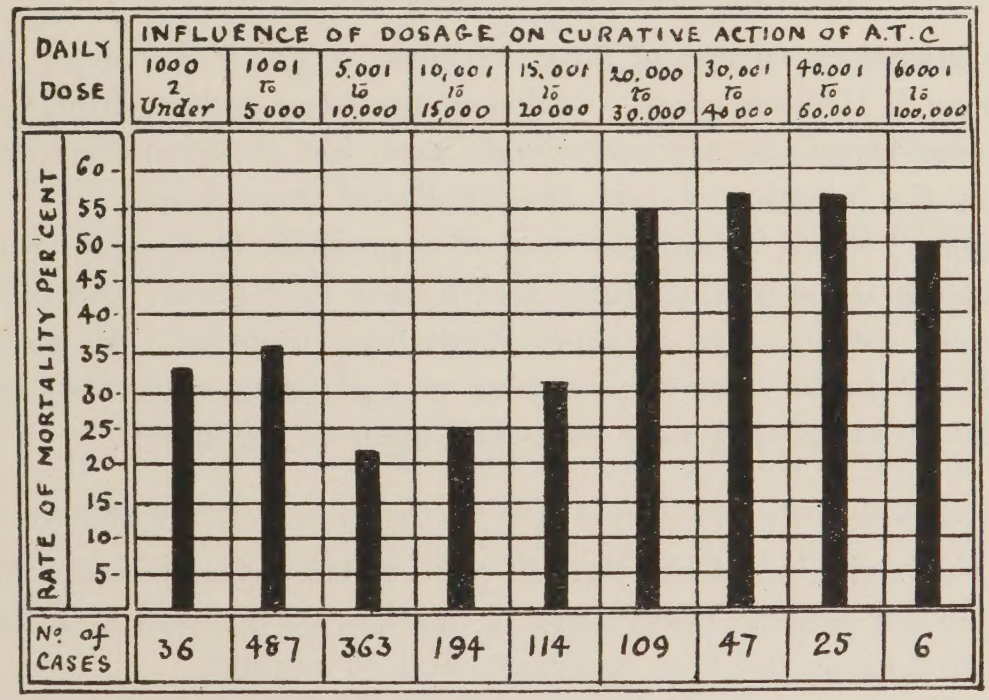


Diagram 12. The average daily dose of antitoxin in home military hospitals.

It is quite evident that no deduction as to the value of antitetanic serum as a therapeutic agent can be made from these premises. At present then the position seems to be this: antitoxin has no power of neutralising toxin in the nervous system. If a fatal amount has been absorbed then no amount of antitoxin will save the man's life. If there is any free toxin circulating in

the blood or lymph the antitoxin may neutralise it and so possibly prevent further mischief. If then a fatal amount has not been absorbed by the nerve cells, the injection of antitoxin may be of use. By animal experiment it appears to be proved that the intrathecal route is the best. Therefore the Tetanus Committee in the fourth edition of the Memorandum on Tetanus recommended antitoxin intrathecally at the first sign of tetanus.

IX. TYPES OF TETANUS BACILLI.

Major Tulloch, a member of the Tetanus Committee, worked with the greatest industry in order to obtain pure cultivations of the tetanus bacilli with a view to separating and studying the different strains. By means of agglutination tests he has separated them into four types. It was expected that each type would be specific to its own serum, but this was found not to be the case. Antitoxin prepared from any one of the types is stated to neutralise the toxins of all the types. It appears that in the past, tetanus antitoxin has been as a rule prepared from Tulloch's type 1 bacillus, but now as the result of his work it is usual in England to inject the horses with toxins from all four types. This subject is admittedly in its infancy and Tulloch's papers should be consulted for fuller information.

X. ANAPHYLAXIS.

Anaphylactic shock after prophylactic injections.

These injections consist of 3 c.c. of horse serum if 500 units are given; of 9 or 10 c.c. if 1500 are given:—serious symptoms resulting from these small subcutaneous injections are exceedingly rare, but occasionally severe shock may follow the injection of even the smaller of these doses.

In England alone, during the war, it is probable that some two millions of prophylactic doses of antitetanic serum have been given. Out of this huge number only eleven cases of shock have been reported. All eleven cases recovered. No doubt these cases appear very alarming when they occur, but they are so rare that they may be looked upon as negligible.

Anaphylactic shock following the therapeutic use of serum.

Since the beginning of the war, 49 cases of anaphylactic shock have been notified (3·5 per cent.). There were 12 deaths (0·8 per cent.). Fifteen cases were reported as severe, 6 as moderate, and 16 as mild.

Of the 49 cases of shock, 17 were caused by intrathecal injections, 14 by intravenous, 9 by intramuscular and 2 by subcutaneous. In 7 it is doubtful which injection caused the shock. Of the whole number of cases of tetanus, 757 received intrathecal, 232 intravenous, 736 intramuscular and 819 subcutaneous injections.

It follows then that 2 per cent. of the cases of shock followed the intrathecal injections, 6 per cent. the intravenous, 1·2 per cent. the intramuscular and

0·2 per cent. the subcutaneous route of injection. It is evident from these figures that the most dangerous route for the therapeutic injection of anti-tetanic serum is the intravenous, and that the Tetanus Committee were justified in not recommending it.

From this it will be seen that anaphylactic shock after therapeutic injections of antitetanic serum is by no means a rare phenomenon, and markedly reduces the questionable usefulness of therapeutic serum.

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